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# $^{125}$I brachytherapy combined with chemotherapy of advanced non-small cell lung cancer*

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This study was to evaluate effect of $^{125}$I brachytherapy combined with chemotherapy on advanced non-small cell lung cancer (NSCLC). Patients with NSCLC in stages III to IV were divided into two groups: Group A ($n = 27$) received $^{125}$I brachytherapy combined with gemcitabine and cisplatin (GP) chemotherapy, and Group B ($n = 27$) received GP chemotherapy only. The results showed that the overall response rate and median progression-free survival time were 78% and 11.5 months in Group A, 41% and 8 months in Group B, respectively ($P < 0.05$). For Group A, the 1- and 2-years survival rates were 67% and 37%, respectively, with the median survival time of 16 months, whereas the corresponding data of Group B were 48%, 22% and 11.5 months ($P > 0.05$). The interventional complications in Group A included 5 patients with postoperative pneumothorax and 4 patients with hemoptysis. No patients had radiation pneumonia, radiation esophagitis or esophagotracheal fistula. Chemotherapy treatment-related toxicities were not significantly different between the two groups. The relief of tumor-associated symptoms including cough, hemoptysis, chest pain, and short breath was found in both groups, without statistical difference in remission rates between Groups A and B ($P > 0.05$). In conclusion, $^{125}$I brachytherapy combined with chemotherapy proved to be safe and effective for treating advanced NSCLC with few complications. It improves local control rate and prolongs the progression-free survival time.

Keywords: Non-small cell lung cancer, $^{125}$I brachytherapy, Chemotherapy

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## I. INTRODUCTION

Lung cancer is the leading cause of cancer-related mortality, about 80%–85% of which are non-small cell lung cancer (NSCLC) [1–3]. The treatment is dominated by surgery, but due to the lack of typical symptoms in the early stages, up to 70% of patients with NSCLC already have locally advanced or metastatic disease at the time of diagnosis. This is why only a third of all patients are eligible to receive curative treatment, hence the poor overall prognosis [4, 5]. To some extent, radiation treatment can alleviate the clinical symptoms of NSCLC in the middle and advanced stages, but the overall effect is not satisfying [6]. Chemotherapy is the mainstay of treatment for NSCLC in the middle and advanced stages, among which gemcitabine and cisplatin (GP) are the standard regimen [7]. However, the local control rate of chemotherapy and its effect on distant metastases are still not actually ideal due to the imperfect tissues distribution [8].

Iodine-125 decays, in half-life of $T_{1/2} = 59.6$ d, through electron capture into excited tellurium-125, which emits low energy $\gamma$-rays (27–35.5 keV, actually they are the 35.5 keV $\gamma$-ray and tellurium $K_\alpha$ and $K_\beta$ X-rays induced by the 35.5 keV $\gamma$-ray). This can be used in low dose rate brachytherapy by implanting $^{125}$I seeds in the tumor area. In treatments of lung carcinoma, $^{125}$I seeds cause little trauma, less complications and favorable local control rate [9–11]. In this study, efficacy and feasibility of $^{125}$I brachytherapy combined with chemotherapy on advanced NSCLC were evaluated.

## II. SUBJECTS AND METHODS

### A. Subjects

From February 2010 to January 2012, 54 patients treated in China-Japan Union Hospital affiliated to Jilin University were enrolled in this study.

The inclusion criteria were: a) patients with histologically confirmed NSCLC in stages III to IV according to the International Union Against Cancer staging system and ineligible for surgical resection [12]; b) Karnofsky performance status of 70 or more; c) no severe coagulation disorders; and d) a life expectancy of more than 3 months.

They did not include those patients who were in pregnancy or lactation (a), who had received anti-tumor treatment such as chemotherapy, radiotherapy or other anti-tumor therapy within 3 months of study treatments (b), who were suffering from uncontrolled serious infections (c), and who were suffering a concomitant serious illness, such as uncontrolled angina pectoris, myocardial infarction within 3 months, heart failure, uncontrolled diabetes mellitus, severe respiratory failure, uncontrolled hypertension and severe coagulation disorders (d).

The 54 patients were divided into two groups: $^{125}$I brachytherapy combined with GP chemotherapy (Group A, $n = 27$), and GP chemotherapy only (Group B, $n = 27$).

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Informed written consent to participate was obtained from all patients. The study protocol was approved by the Ethics Committee and the Institutional Review Board of China-Japan Union Hospital, Changchun, China.

### B. $^{125}$I seed implantation

The $^{125}$I seeds were Model BT-125-1, GMS Pharmaceutical Co., LTD, Shanghai, China, sized at $(4.5 \pm 0.5)$ mm length and $(0.80 \pm 0.05)$ mm thick, with an initial activity of 25.9 MBq. Before implanting the $^{125}$I seed, Group A patients underwent Single-Photon Emission Computed Tomography/CT (SPET/CT, Philips Healthcare, WA) scanning to evaluate the form, volume and features of the tumor. The CT images of 5 mm layer thickness were input into the treatment-planning system (TPS) produced by Beijing Flying Zhaoye Technology Co., LTD. The minimum prescribed dose tumor value (MPD) was 120 Gy (100–140 Gy). According to the preoperative plan made by TPS, the required number and location of the $^{125}$I seeds were determined and the needle's position was marked on the patien's body surface. Implantation was carried out by professional radioactive technicians under the guidance of CT. With 2% lidocaine local anesthesia, one or multiple 18-gauge needles were gradually inserted percutaneously into the tumor, and the turntable implantation gun was applied to implant $^{125}$I seeds into the tumor at 0.5–1.0 cm intervals. The adjacent implantation needles were gapped at about 1 cm. The $^{125}$I seeds were implanted as planned and instant verification was made by CT scanning.

### C. Chemotherapy

Chemotherapy consisting of gemcitabine (1000 mg/m$^2$ on Day 1 and 8) and cisplatin (30 mg/m$^2$ on Day1, 2 and 3) applied to all patients intravenously. The GP chemotherapy was repeated every 3 weeks with a maximum of 4 cycles. Before chemotherapy, patients were routinely given 5-HT$_3$ antagonist for prevention of vomiting response. If a patient experienced excessive adverse events, the subsequent treatment cycle would be delayed until the events almost disappeared.

### D. Follow-up and evaluation

Before treatment, the vital signs and tumor-associated symptoms of the patients (cough, hemoptysis, chest pain, and short breath) were recorded. Follow-up CT examinations and clinical hematological tests were performed monthly for the first 3 months and then at 1–3 months interval.

Tumor response, evaluated according to the Response Evaluation Criteria in Solid Tumors (RECIST), was classified as follows: complete response (*CR*), partial response (*PR*), stable disease (*SD*) and progressive disease (*PD*). The overall response rate (*ORR*) was calculated as the total percentage of patients with a *CR* and *PR*. The clinical effects of treatment were assessed by *ORR*, progression-free survival time (PFST), survival time (ST), and treatment-related adverse effects.

### E. Statistical analysis

The statistical analysis was performed using SPSS 19.0 statistical software. The data are presented as the mean $\pm$ standard deviation (*SD*). Significance of differences was evaluated by Student's $t$ test. Response to treatment was analyzed by Pearson's $\chi^2$ test. Survival analysis was done with the Kaplan-Meier method, and the log-rank test was used for survival comparison. Values with $P < 0.05$ were considered statistically significant.

## III. RESULTS

### A. Patient and tumor characteristics

From February 2010 to January 2012, a total of 54 patients with unresectable stage III to IV NSCLC were recruited in this study. Group A ($n = 27$) were assigned to combined $^{125}$I brachytherapy and GP chemotherapy, and Group B ($n = 27$) were assigned to GP chemotherapy only. The median follow-up time was 15 months (range 5–28 months). Average chemotherapy cycles were $2.4 \pm 0.8$ in Group A and $2.7 \pm 0.9$ in Group B ($P > 0.05$). The verified dose for Group A was $(123.4 \pm 10.7)$ Gy, being consistent with the treatment requirements. Patients' characteristics are given in Table 1. There was no statistical difference in age, gender, histology, lesion location, clinical stage and tumor size between the two groups ($P > 0.05$).

TABLE 1. Characteristics of enrolled patients with advanced NSCLC

| Characteristics[a] | Group A ($n = 27$) | Group B ($n = 27$) |
|---|---|---|
| Age/y (mean $\pm SD$ ) | 45–68(60 $\pm$ 8.5) | 51–70(64 $\pm$ 7.4) |
| Gender (male/female) | 17/10 | 13/14 |
| Histology(S/A/AC) [b] | 16/9/2 | 19/5/3 |
| Lesion location (C/P) [c] | 20/7 | 16/11 |
| Clinical stage (III/IV) | 16/11 | 13/14 |
| Tumor size /cm | $4.1 \pm 2.1$ | $3.9 \pm 2.5$ |

[a] No statistical difference was found in age, gender, histology, lesion location, clinical stage and tumor size between the two groups ($P > 0.05$).
[b] S, squamous; A, adenocarcinoma; AC, adenosquamous carcinoma.
[c] C, center type; P, peripheral type.

### B. Anti-tumor efficacy

In Group A, *CR*, *PR*, *SD* and *PD* were observed in 5, 16, 4, and 2 patients, respectively. A typical case of complete response in Group A is shown in Fig. 1. In Group B, *CR*, *PR*, *SD* and *PD* were observed in 2, 9, 9, and 7 patients, respectively. The *ORR* (*CR* + *PR*) in 6 months were 78% for Group



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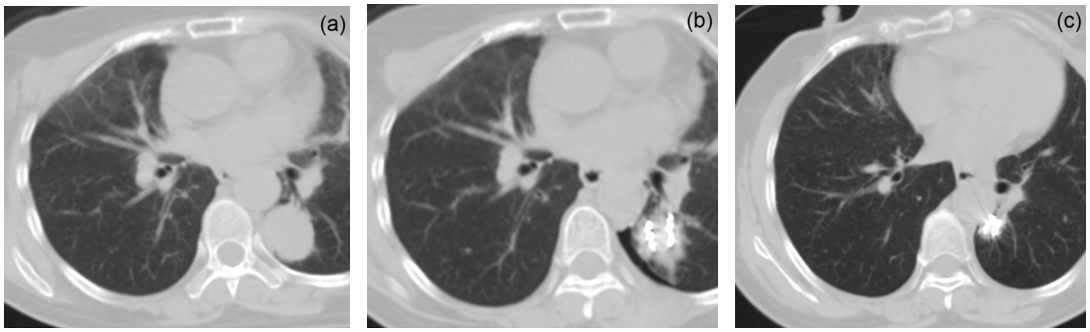


Fig. 1. A typical case of $^{125}$I brachytherapy and GP chemotherapy treatments: a 60-years-old man with squamous cell cancer located in the lower lobe of left lung, (a) The tumor was sized at 4.2 cm × 4.0 cm. (b) Instant CT scan verification was made after implanting $^{125}$I seeds and the verified dose was 116.8 Gy. (c) Six month after $^{125}$I brachytherapy and GP chemotherapy, the lesion disappeared on the CT scan, only funicular shadow and the $^{125}$I seeds left. The patient achieved complete response after the treatments.

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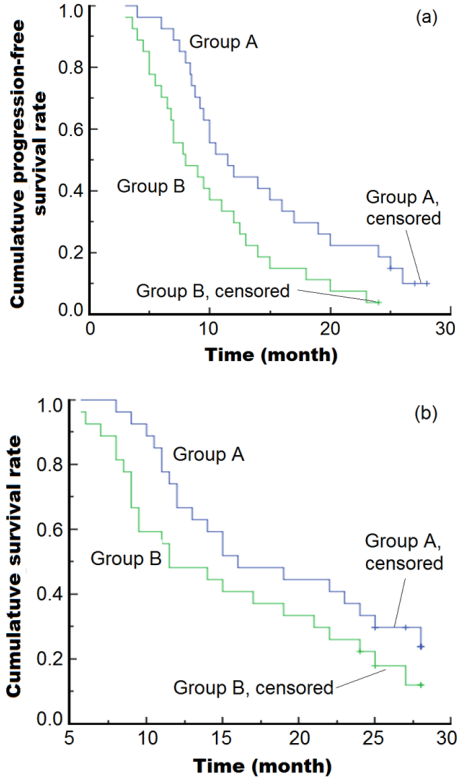


Fig. 2. (Color online) Progression-free survival time (a) and overall survival rate (b) in Groups A and B. Group A is better than Group B in progression-free survival time ($P = 0.023$), but no statistical difference was observed in the overall survival rates ($P = 0.125$).

A and 41% for Group B ($P < 0.05$; Table 2). The median PFST was 11.5 months in Group A and 8 months in Group B ($P < 0.05$; Fig. 2(a)). The median ST was 16 months in Group A and 11.5 months in Group B ($P > 0.05$; Fig. 2(b)). The 1- and 2-year survival rates were 67% and 37% in Group A and 48% and 22% in Group B, respectively. No statistically significant difference in survival rates was found between the two groups ($P > 0.05$), while significant difference in *ORR*

TABLE 2. Curative effects in Group A and Group B

| | *CR* | *PR* | *SD* | *PD* | *ORR* (%) |
|---|---|---|---|---|---|
| Group A ($n = 27$) | 5 | 16 | 4 | 2 | 77.8 |
| Group B ($n = 27$) | 2 | 9 | 9 | 7 | 40.7 |

[a] *CR*, complete response; *PR*, partial response; *SD*, stable disease; *PD*, progressive disease; *ORR*, overall response rate.

between Group A and Group B was observed ($P < 0.05$).

### C. Complications

No treatment-related death occurred in both groups. In Group A, 5 patients developed postoperative pneumothorax during the $^{125}$I seed implantation procedures. Among them, 4 patients recovered in 2 h, and one who had lung compression $> 30\%$ was treated with thoracic cavity closed drainage and recovered in 2 days. Four patients with hemoptysis recovered after conservative treatment. None of the patients had radiation pneumonia, radiation esophagitis or esophagotracheal fistula during the follow-up.

### D. Adverse events of chemotherapy

Chemotherapy treatment-related toxicities in all the patients were classified based on the WHO toxicity criteria. Grades 3 and 4 leukopenia, thrombocytopenia and anemia were observed in 5, 3, and 2 patients in Group A and 6, 2 and 3 patients in Group B, respectively ($P > 0.05$). Grade 3 nausea/vomiting and diarrhea were observed in 3 and 2 patients in Group A, 4 and 1 patients in Group B, respectively ($P > 0.05$). Grade 3 or 4 arrhythmia, alopecia, liver or renal function damage were not found in both groups.

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### E. Tumor-associated symptoms

Tumor-associated symptoms, such as cough, hemoptysis, chest pain, and short breath, were compared between the two groups before and after treatment. Relief of symptoms associated with the tumor lesions was found in both groups after the treatment in different degrees. The remission rates of cough, hemoptysis, chest pain, and short breath were 60.0% (9/15), 64.3% (9/14), 61.1% (11/18) and 60.0% (12/20) in Group A, 35.3% (6/17), 36.4% (4/11), 35.0% (7/20) and 38.9% (7/18) in Group B, respectively. No statistical difference was found in remission rates between the two groups ($P > 0.05$; Table 3).

TABLE 3. Clinical symptoms before and after treatment in two groups

| Symptoms | Group A ($n = 27$) | | Group B ($n = 27$) | |
|---|---|---|---|---|
| | Before | After | Before | After |
| Cough | 15 | 6 | 17 | 11 |
| Hemoptysis | 14 | 6 | 11 | 7 |
| Chest pain | 18 | 7 | 20 | 13 |
| Short breath | 20 | 8 | 18 | 11 |

## IV. DISCUSSION

The mechanism of $^{125}$I brachytherapy is the use of low energy $\gamma$-rays to damage DNA duplexes and reduce probability of mitosis and of proliferation of cancer cells [9, 13]. By using advanced TPS system we simulated the three-dimensional shape of the tumor and calculated $^{125}$I seeds distribution and therapeutic dose according to tumor morphology. The $^{125}$I seeds were implanted into the tumor under ultrasound, CT or endoscopic guidance providing steady irradiation to the tumor cells at all stages of the cell cycle, with a lower radiation dose to normal tissues adjacent to the lesion. Several studies have proved effectiveness of $^{125}$I brachytherapy of head and neck cancer, pancreatic cancer and prostate cancer [14–18]. Chemotherapy is the mainstay of treatment for advanced NSCLC, of which GP is a standard regimen [7]. The $^{125}$I brachytherapy improves the local control rate, and chemotherapy has a potential effect on distant metastases.

Similar to Refs. [19, 20], combined $^{125}$I brachytherapy with GP chemotherapy can achieve better overall response rate and longer PFST than the control group ($P < 0.05$). Also, the combined treatments showed better benefit in median ST and survival rates, though the results were not statistically significant.

The main complications of $^{125}$I brachytherapy were pneumothorax and hemoptysis [21–24]. In the present study, 5 patients developed postoperative pneumothorax and 4 patients had hemoptysis in the puncture course. All of them recovered after proper treatment. This was compatible with the results in Refs. [21–24]. For both groups, the treatments were well tolerated by patients, without treatment-related death. Due to the low energy spectrum of $^{125}$I, much less radiation damage can be done to neighboring organs. With a median follow-up time of 15 months (in a range of 5–28 months), none of the patients had radiation pneumonia, radiation esophagitis or esophagotracheal fistula. Chemotherapy treatment-related toxicities of Group A were similar to Group B, indicating that $^{125}$I brachytherapy combined with systemic chemotherapy do not increase chemotherapy toxicities, while obtaining good local tumor control.

For patients with advanced NSCLC, the therapeutic goals are not only improving response rate and prolonging life, but also alleviating symptoms and improving quality of life [25]. About 74% of patients with advanced lung carcinoma experience chest pain symptoms [26]. $^{125}$I brachytherpy can relieve chest pain. The mechanisms, not fully understood so far, though, may be related to the decrease of pain chemical mediators because the radiation treatment shrinks tumors or inhibits tumor cells from releasing pain medium [27]. Relief of tumor-associated symptoms including cough, hemoptysis, chest pain, and short breath was found in both groups, without statistical difference in remission rates between the two groups, owing probably to the small sample sizes.

Therefore, further research with more patients is necessary. Also, the observation time (median 15 months) was relatively short, and observations of long-term curative effect, survival time and other indicators should be carried out. Finally, $^{125}$I seeds are of relatively high cost that cannot be accepted by all the patients.

[1] Siegel R, Naishadham D and Jemal A. Cancer statistics, 2013. CA-Cancer J Clin, 2013, **63**: 11–30. DOI: 10.3322/caac.21166

[2] Yu E, Lewis C, Luisa T A, *et al*. Lung cancer brachytherapy: robotics-assisted minimally invasive approach. Curr Respir Med Rev, 2011, **7**: 340–353. DOI: 10.2174/157339811797189803

[3] Jemal A, Bray F, Center M M, *et al*. Global cancer statistics. Global cancer statistics. CA-Cancer J Clin, 2011, **61**: 69–90. DOI: 10.3322/caac.20107

[4] Zhao N, Zhang X, Yan H, *et al*. Efficacy of epidermal growth factor receptor inhibitors versus chemotherapy as second-line treatment in advanced non-small-cell lung cancer with wild-type EGFR: a meta-analysis of randomized controlled clinical trials. Lung Cancer, 2014, **85**: 66–73. DOI: 10.1016/j.lungcan.2014.03.026

[5] Spiro S G, Gould M K and Colice G L. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes: ACCP evidenced-based clinical practice guidelines (2nd edition). Chest, 2007, **132**: 149S–160S. DOI: 10.1378/chest.07-1358

[6] Scott C L, Zalcberg J R and Irving L B. Treatment principles in advanced non-small-cell lung cancer. Aust NZ J Surg, 1996, **66**: 688–693. DOI: 10.1111/j.1445-2197.1996.tb00719.x

[7] Gebbia V, Galetta D, Caruso M, *et al*. Gemcitabine

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and cisplatin versus vinorelbine and cisplatin versus ifosfamide+gemcitabine followed by vinorelbine and cisplatin versus vinorelbine and cisplatin followed by ifosfamide and gemcitabine in stage IIIB–IV non small cell lung carcinoma: a prospective randomized phase III trial of the Gruppo Oncologico Italia Meridionale. Lung Cancer, 2003, **39**: 179–189. DOI: 10.1016/S0169-5002(02)00444-0

[8] Moreno-Jiménez M, Aristu J, López-Picazo J M, *et al*. Dosimetric analysis of the patterns of local failure observed in patients with locally advanced non-small cell lung cancer treated with neoadjuvant chemotherapy and concurrent conformal (3D-CRT) chemoradiation. Radiotherapy Oncol, 2008, **88**: 342–350. DOI: 10.1016/j.radonc.2008.05.019

[9] Martínez-Monge R, Pagola M, Vivas I, *et al*. CT-guided permanent brachytherapy for patients with medically inoperable early-stage non-small cell lung cancer (NSCLC). Lung Cancer, 2008, **61**: 209–213. DOI: 10.1016/j.lungcan.2007.12.016

[10] Hu X K, Qiu H J, Zhang L, *et al*. Recurrent gliomas: comparison of computed tomography (CT)-guided 125I seed implantation therapy and traditional radiochemotherapy. Cancer Biol Ther, 2012, **13**: 840–847. DOI: 10.4161/cbt.20834

[11] Chang C Y, Chang S J, Chang S C, *et al*. The value of positron emission tomography in early detection of lung cancer in high-risk population: a systematic review. Clin Respir J, 2013, **7**: 1–6. DOI: 10.1111/j.1752-699X.2012.00290.x

[12] Egner J R. AJCC cancer staging manual. JAMA-J Am Med Assoc, 2010, **304**: 1726–1727. DOI: 10.1001/jama.2010.1525

[13] Ma J X, Jin Z D, Si P R, *et al*. Continuous and low-energy $^{125}$I seed irradiation changes DNA methyltransferases expression patterns and inhibits pancreatic cancer tumor growth. Exp Clin Cancer Res, 2011, **30**: 35. DOI: 10.1186/1756-9966-30-35

[14] Jiang Y L, Meng N J, Ran W Q, *et al*. Percutaneous computed tomography/ultrasonography-guided permanent iodine-125 implantation as salvage therapy for recurrent squamous cell cancers of head and neck. Cancer Biol Ther, 2010, **9**: 959–966. DOI: 10.4161/cbt.9.12.11700

[15] Hinnen K A and Marco V V. Predictors in the outcome of 125I brachytherapy as monotherapy for prostate cancer. Expert Rev Anticanc, 2011, **11**: 115–123. DOI: 10.1586/era.10.211.

[16] Konaka H, Egawa S, Saito S, *et al*. Tri-Modality therapy with I-125 brachytherapy, external beam radiation therapy, and short- or long-term hormone therapy for high-risk localized prostate cancer (TRIP): study protocol for a phase III, multicenter, randomized, controlled trial. BMC Cancer, 2012, **12**: 110. DOI: 10.1186/1471-2407-12-110

[17] Jin Z, Du Y, Li Z, *et al*. Endoscopic ultrasonography-guided interstitial implantation of iodine 125-seeds combined with chemotherapy in the treatment of unresectable pancreatic carcinoma: a prospective pilot study. Endoscopy, 2008, **40**: 314–320. DOI: 10.1055/s-2007-995476

[18] Wang J, Jiang Y, Li J, *et al*. Intraoperative ultrasound-guided iodine-125 seed implantation for unresectable pancreatic carcinoma. J Exp Clin Cancer Res, 2009, **28**: 88. DOI: 10.1186/1756-9966-28-88

[19] Ke Q, Fu G, Bian Y, *et al*. Concurrent gemcitabine and cisplatin combined with 3D conformal radiotherapy for stage III non-small cell lung cancer. Chin-Ger J Clin Oncol, 2009, **8**: 156–159. DOI: 10.1007/s10330-008-0164-2

[20] Yu X, Li J, Zhong X, *et al*. Combination of Iodine-125 brachytherapy and chemotherapy for locally recurrent stage III non-small cell lung cancer after concurrent chemoradiotherapy. BMC Cancer, 2015, **15**: 656. DOI: 10.1186/s12885-015-1657-3

[21] Brach B, Buhler C, Hayman M H, *et al*. Percutaneous computed tomography-guided fine needle brachytherapy of pulmonary malignancies. Chest, 1994, **106**: 268–274. DOI: 10.1378/chest.106.1.268

[22] Heelan R T, Hilaris B S, Anderson L L, *et al*. Lung tumors: percutaneous implantation of I-125 sources with CT treatment planning. Radiology, 1987, **164**: 735–740. DOI: 10.1148/radiology.164.3.3615870

[23] Martínez-Monge R, Pagola M, Vivas I, *et al*. CT-guided permanent brachytherapy for patients with medically inoperable early-stage non-small cell lung cancer(NSCLC). Lung Cancer, 2008, **61**: 209–213. DOI: 10.1016/j.lungcan.2007.12.016

[24] Guimarães M D, de Andrade M Q, da Fonte A C, *et al*. Predictive complication factors for CT-guided fine needle aspiration biopsy of pulmonary lesions. Clinics, 2010, **65**: 847–850. DOI: 10.1590/S1807-59322010000900006

[25] Paccagnella A, Favaretto A, Oniga F, *et al*. Cisplatin versus carboplatin in combination with mitomycin and vinblastine in advanced non small cell lung cancer. A multicenter, randomized phase III trial. Lung Cancer, 2004, **43**: 83–91. DOI: 10.1016/S0169-5002(03)00280-0

[26] Di Maio M, Gridelli C, Gallo C, *et al*. Prevalence and management of pain in Italian patients with advanced non-small-cell lung cancer. Br J Cancer, 2004, **90**: 2288–2296. DOI: 10.1038/sj.bjc.6601810

[27] Zhang T, Lu M, Peng S, *et al*. CT-guided implantation of radioactive 125I seed in advanced non-small-cell lung cancer after failure of first-line chemotherapy. J Cancer Res Clin Oncol, 2014, **140**: 1383–1390. DOI: 10.1007/s00432-014-1655-x

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